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| Zeichen/Ref./Réf. CMD/FP5894753 | Anmeldung Nr./Application No./Demande n°./Patent Nr./Patent No./Brevet n° 99925874.2-1222/US9911629 |
| Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire Virologic, Inc. | |

# COMMUNICATION

The European Patent Office herewith transmits the partial European search report under Rule 46(1) EPC relating to the above-mentioned European patent application.

Copies of the documents cited in the search report are enclosed.

The applicant's attention is drawn to the following:

The Search Division informs the applicant that if the European search report is also to cover inventions other than the invention first mentioned in the claims, a further search fee must be paid for each of these inventions, within ONE MONTH after notification of this communication.

If the application has been filed up to 30 June 1999, the search fee in force before 01 July 1999 (EUR 869.—) or the equivalent applicable on the date of payment is payable.
**This applies also to the search fees requested under Rule 46(1) EPC.**
See also OJ EPO 06/1999, 405.

☐ The abstract was modified by the Search Division and the definitive text is attached to the present communication.

☒ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

## Note to users of the automatic debiting procedure:

Unless the EPO receives prior instructions to the contrary, the search fee(s) will be debited on the last day of the period for payment. For further details see the Arrangements for the automatic debiting procedure, Supplement to OJ EPO 02/1999.

REGISTERED LETTER

EPO Form 1507.2 (07.99)

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# SUPPLEMENTARY
# PARTIAL EUROPEAN SEARCH REPORT

under Rule 46, paragraph 1 of the European Patent Convention

Application Number
EP 99 92 5874

## DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | CLASSIFICATION OF THE APPLICATION (Int.Cl.6) |
|---|---|---|---|
| X | WO 97/27332 A (INNOGENETICS NV ; STUYVER LIEVEN (BE); LOUWAGIE JOOST (BE); ROSSAU RUD) 31 July 1997 (1997-07-31)<br>* page 4, line 5 - page 5, line 12 *<br>* page 10, line 20 - line 25 *<br>* page 13, line 26 - line 29 *<br>* page 22, line 19 - line 22 *<br>* tables 1,2 *<br>----- | 1-5 | C12Q1/66<br>C12Q1/68<br>C12Q1/70<br>C12P19/34<br>C12N15/00<br>C12N15/64<br>C12N15/85<br>C07H21/04 |
| D,Y | WO 97/27319 A (VIROLOGIC INC) 31 July 1997 (1997-07-31)<br>* claims 1,5,12,28,33 *<br>-----<br>-/-- | 1-8 | |

| TECHNICAL FIELDS SEARCHED (Int.Cl.6) |
|---|
| C12Q |

## LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

The present partial European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims.

| Place of search | Date of completion of the search | Examiner |
|---|---|---|
| The Hague | 15 September 2004 | Schmitt. A |

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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# PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 99 92 5874

## DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | CLASSIFICATION OF THE APPLICATION (Int.Cl.6) |
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| Y | ROMERO D L ET AL: "Targeting delavirdine/atevirdine resistant HIV-1: identification of (alkylamino)piperidine-containing bis(heteroaryl)piperazines as broad spectrum HIV-1 reverse transcriptase inhibitors."<br>JOURNAL OF MEDICINAL CHEMISTRY. 13 SEP 1996,<br>vol. 39, no. 19,<br>13 September 1996 (1996-09-13), pages 3769-3789, XP002295736<br>ISSN: 0022-2623<br>* the whole document *<br>* table 1 *<br>-----<br>-/-- | 1-8 | TECHNICAL FIELDS SEARCHED (Int.Cl.6) |

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EPO FORM 1503 03.82 (P04C10)

# PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 99 92 5874

## DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | CLASSIFICATION OF THE APPLICATION (Int.Cl.6) |
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| Y | BUCKHEIT R W JR ET AL: "Resistance to 1-[(2-hydroxyethoxy)methyl]-6-(phenylthio) thymine derivatives is generated by mutations at multiple sites in the HIV-1 reverse transcriptase."<br>VIROLOGY. 20 JUN 1995,<br>vol. 210, no. 1,<br>20 June 1995 (1995-06-20), pages 186-193, XP002295737<br>ISSN: 0042-6822<br>* the whole document *<br>* tables 2-4 *<br>----- | 1-8 | |
| A | FAN N ET AL: "Mechanism of resistance to U-90152S and sensitization to L-697,661 by a proline to leucine change at residue 236 of human immunodeficiency virus type 1 (HIV-1) reverse transcriptase."<br>FEBS LETTERS. 13 FEB 1995,<br>vol. 359, no. 2-3,<br>13 February 1995 (1995-02-13), pages 233-238, XP002295738<br>ISSN: 0014-5793<br>* the whole document *<br>* figures 3,4 *<br>----- | 1-8 | TECHNICAL FIELDS SEARCHED (Int.Cl.6) |
| A | KANKI P J ET AL: "Virology of HIV-1 and HIV-2: implications for Africa."<br>AIDS (LONDON, ENGLAND) 1997,<br>vol. 11 Suppl B, 1997, pages S33-S42, XP008035289<br>ISSN: 0269-9370<br>* figure 1 *<br>-----<br>-/-- | 1-8 | |

# PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 99 92 5874

| DOCUMENTS CONSIDERED TO BE RELEVANT | | | CLASSIFICATION OF THE APPLICATION (Int.Cl.6) |
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| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | |
| A | ESNOUF R M ET AL: "Unique features in the structure of the complex between HIV-1 reverse transcriptase and the bis(heteroaryl)piperazine (BHAP) U-90152 explain resistance mutations for this nonnucleoside inhibitor."<br>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. 15 APR 1997,<br>vol. 94, no. 8,<br>15 April 1997 (1997-04-15), pages 3984-3989, XP002295739<br>ISSN: 0027-8424<br>* the whole document *<br>----- | 1-8 | |
| A | MELLORS J W ET AL: "MUTATIONS IN HIV-1 REVERSE TRANSCRIPTASE AND PROTEASE ASSOCIATED WITH DRUG RESISTANCE"<br>INTERNATIONAL ANTIVIRAL NEWS, CHURCHILL LIVINGSTONE, EDINBURGH, GB,<br>vol. 3, 1995, pages 8-13, XP000614717<br>ISSN: 0965-2310<br>* the whole document *<br>----- | 1-8 | TECHNICAL FIELDS SEARCHED (Int.Cl.6) |

European Patent Office

# LACK OF UNITY OF INVENTION
## SHEET B

Application Number
EP 99 92 5874

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. claims: 1-8 (partially)

Method for assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising evaluating whether a patient plasma sample contains nucleic acid encoding HIV reverse transcriptase (HIV-RT) having a mutation at codon 236 or at codons 236 and 103, 181 or a combination thereof; and method and resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at codon 236 or at codon 236 and 103, 181 or a combination thereof.

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2. claims: 1-8 (partially)

Method for assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising evaluating whether a patient plasma sample contains nucleic acid encoding HIV-RT having a mutation at codon 225 or codons 225 and 103, 181 or a combination thereof; and method and/or resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at said codons.

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3. claims: 1-8 (partially)

Method for assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising evaluating whether a patient plasma sample contains nucleic acid encoding HIV-RT having a mutation at codon 190 or codons 190 and 89, 101, 103 or a combination thereof; and method and/or resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at said codons.

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4. claims: 1-8 (partially)

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

Method for assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising evaluating whether a patient plasma sample contains nucleic acid encoding HIV-RT having a mutation at codon 230 or codons 230 and 181; and method and/or resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at said codons.

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5. claims: 1-8 (partially)

Method for assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising evaluating whether a patient plasma sample contains nucleic acid encoding HIV-RT having a mutation at codon 188 or codons 188 and 138, 103, 100 or a combination thereof; and method and/or resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at said codons.

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6. claims: 1-7 (partially)

Method for assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising evaluating whether a patient plasma sample contains nucleic acid encoding HIV-RT having a mutation at codon 181 or codons 181 and 98, 106, 227 or a combination thereof; and method and/or resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at said codon(s).

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7. claims: 1-7 (partially)

Method for assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising evaluating whether a patient plasma sample contains nucleic acid encoding HIV-RT having a mutation at codon 106 or codons 106 and 227, 189 or a combination thereof; and method and/or resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at said codon(s).

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

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8. claims: 1-7 (partially)

   Method for assessing the effectiveness of non-nucleoside reverse transcriptase antiretroviral therapy of an HIV-infected patient comprising evaluating whether a patient plasma sample contains nucleic acid encoding HIV-RT having a mutation at codon 103 or codons 103 and 100; and method and/or resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at said codon(s).

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9. claims: 6,7 (partially)

   Method and resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at codon 227.

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10. claims: 6,7 (partially)

    Method and resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at codon 189.

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11. claim: 7 (partially)

    Resistance test vector for assessing the biological effectiveness of a candidate HIV antiretroviral drug compound comprising a patient-derived segment [of reverse transcriptase] which comprises a mutation at codons 103 and 101.

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The single general concept that may possibly link inventions 1 to 11 listed above, as required by Rule 30 EPC, appears to be the provision of methods and/or products for assessing drug effectiveness involving HIV-RT having a mutation at a certain codon.
Methods and/or products for assessing drug effectiveness involving HIV-RT having a mutation at a certain codon are already disclosed in the prior art (cf. WO97/27332 A: p. 4, l. 15 - p. 5, l. 6; Tables 1 and 2; cf. Dueweke et al (1993): Table 1; Fig. 2; p. 4713, co. 2, par. 2 - p. 4714, co. 2, par. 2; cf. Romero et al (1996): Table 1; p. 3787, co. 1, par. 5 -

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

col. 2, par. 3; cf. : De Clercq (1997): Tables 4 and 5).
Therefore, the above defined single general concept lacks novelty and thus does not represent a single general inventive concept. Hence, the present application lacks unity (Art. 82 EPC).

# ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO.

EP 99 92 5874

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
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15-09-2004

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| | | | AU | 1444397 | A | 20-08-1997 |
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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

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